IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Docket No.: 31927-CIP2
MESSADEK, Jallal	
Patent No.: 7,608,640	
Application No.: 10/635,048	Group Art Unit No.: 1617
Issued: October 27, 2009	Customer No.: 23589
GLYCINE BETAINE AND ITS USE	Examiner: Betton, Timothy E.

Commissioner for Patents
Office of Patent Publication
Attn: Certificate of Correction Branch
P.O. Box 1450
Alexandria, Virginia 22313-1450

REQUEST FOR CORRECTION UNDER 37 C.F.R. § 1.322

Applicant hereby petitions the Office under 37 C.F.R. § 1.322 to issue a Certificate of Correction for the Patent Office's mistake in U.S. Patent No. 7,608,640. The mistake consists of typographical errors in Claims 2 and 15. As set forth in Form PTO/SB/44, submitted herewith, the phrase "control led" in claim 2, line 15, should now read "controlled," and the word "flaw" in claim 15, line 38, should now read "flow."

Applicant requests expedited issuance of the Certificate of Correction under 37 C.F.R. § 1.322. Furthermore, to demonstrate that the error is attributable solely to the Office, Applicant has attached the relevant documentation showing that the claims were in correct form when last submitted by Applicant to the Office in an Amendment After Final, dated October 22, 2008. Claim 2 of the '640 patent corresponds to claim 15 in the Amendment After Final, where it is clear that "controlled" was written as one word. Claim 15 of the '640 patent corresponds to claim 42 in the Amendment After Final, where it is clear that the word "flow," and not "flaw" was recited in Applicant's claim. Applicant has also attached the Notice of Allowability, dated

June 12, 2009, which included an Examiner's Amendment. No further amendments have been made to the claims.

Therefore, in accordance with M.P.E.P. § 1480.01, the records of the Office, as evidenced by the attached documentation, unequivocally support the Applicant's assertion that the requested correction was incurred through the fault of the Office. Moreover, Applicant submits that issuance of a Certificate of Correction correcting these errors in the above-referenced patent will not involve any changes constituting new matter or requiring reexamination. Accordingly, the expedited issuance of a Certificate of Correction is proper in this instance and the same is respectfully requested.

It is believed that no fee is due for this submission to correct the Patent Office's mistake under 37 C.F.R. § 1.322. However, any such fees which are due should be applied against Deposit Account No. 19-0522.

Respectfully submitted,

By Tracy Bornman by [illegible] Reg No 64,054

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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 7,608,640

APPLICATION NO.: 10/635,048

ISSUE DATE : October 27, 2009

INVENTOR(S) : Messadek, Jallal

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Claim 2, line 15, the word "control led" should read --controlled--;

Claim 15, line 38, the word "flaw" should read --flow--.

MAILING ADDRESS OF SENDER (Please do not use customer number below):

Hovey Williams LLP
10801 Mastin Blvd., Suite 1000
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This collection of information is required by 37 CFR 1.322, 1.323, and 1.324. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1.0 hour to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Attention Certificate of Corrections Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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Ele onic Acknowledgement Rece

EFS ID:	4159967
Application Number:	10635048
International Application Number:	
Confirmation Number:	6961
Title of Invention:	Glycine betaine and its use
First Named Inventor/Applicant Name:	Jallal Messadek
Customer Number:	23589
Filer:	Tracy L. Bornman/Jean Kahrau
Filer Authorized By:	Tracy L. Bornman
Attorney Docket Number:	31927-CIP2
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Time Stamp:	17:48:59
Application Type:	Utility under 35 USC 111(a)

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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		Amendmentnreponseto08-06-08OfficeAction.pdf	2212457 e0bfe9f3b618c45671fec0874da2476b98095ffs	yes	30

Multipart Description/PDF files in .zip description		
Document Description	**Start**	**End**
Amendment/Req. Reconsideration-After Non-Final Reject	1	1
Claims	2	12
Applicant Arguments/Remarks Made in an Amendment	13	30

Warnings:

Information:

Total Files Size (in bytes):	2212457

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Docket No.: 31927-CIP2
MESSADEK, Jallal	Confirmation No.: 6961
Serial No.: 10/635,048	Group Art Unit No.: 1617
Filed: August 4, 2003	Customer No.: 23589
GLYCINE BETAINE AND ITS USE	Examiner: Betton, Timothy E.

Commissioner for Patents
Mail Stop Amendment
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

OFFICE ACTION RESPONSE

In response to the Office Action dated August 6, 2008, amendment and reconsideration of the above application is requested.

The claim amendments begin on page 2.

Remarks/Arguments begin on page 13.

Claims:

1. (Withdrawn) A pharmaceutical antithrombotic combination comprising:

(a) a therapeutically effective amount of a therapeutically antithrombotic active agent causing at least one haemorrhagic side effect, said active agent being selected from the group consisting of anti aggregants selected from the group consisting of abciximab, acetylsalicylate basic aluminium, acetylsalicylate carbonate sodium, acetylsalicylate lysine, acetylsalicylic acid, aloxiprine, anagreli chlorydrate, bencyclane furamate, carbasalate calcium, clopidogrel sulfate, epoprostenol sodium, epifibati, hydroxychloroquine sulfate, iloprost, nicergoline, nifepidine, pyricarbate, sulfinpyrazone, ticlopidine chlorhydrate, tirofiban chlorhydrate, verapamil chlorhydrate, compounds structurally similar to one of said preceding anti aggregant compounds, and mixtures thereof, anticoagulants selected from the group consisting of acenocoumarol, anisindione, biscoumacetate ethyl, bromindione, coumetarol, sirudine, oxazidione, phenindione, phenprocoumone, tioclomarol, warfarine sodium, compounds structurally similar to one of the preceding anti coagulant compounds, and mixtures thereof, fibrinolytics selected from the group consisting of altepase, anistreplase, atorvastatine calcium, bromelaines, ciprofibrate, defibrotide, fluvastatine sodium, glicazide, lovastatine, lys-plasminogene, phenformine, pravastatine sodium, reteplase, simvastatine, streptokinase, urokinase, compounds structurally similar to one of the preceding fibrinolytic compounds, and mixtures thereof, thrombin inhibitors, anti vitamin K, and mixtures thereof; and

(b) a therapeutically effective amount of a compound selected from the group consisting of compounds of the formula $(CH_3)_3N^+(CH_2)_nCOO^-$ with n an integer from 1 to 5, pharmaceutically acceptable salts thereof, esters thereof, precursors thereof, and mixtures thereof,

said combination operable for preventing or reducing the incidence or severity of said haemorrhagic side effect or for potentialising the therapeutic antithrombotic effect of said antithrombotic active agent.

2. (Withdrawn) The pharmaceutical combination of claim 1, said compound being selected from the group consisting of glycine betaine, pharmaceutically acceptable salts thereof, esters thereof, precursors thereof, and mixtures thereof.

3. (Withdrawn) The pharmaceutical combination of claim 1, in which the therapeutic antithrombotic active agent has at least possible haemorrhagic side effects, and in which the combination comprises a therapeutically effective amount of glycine betaine for preventing or reducing the incidence or severity of said haemorrhagic side effect.

4. (Withdrawn) The pharmaceutical combination of claim 3, in which said glycine betaine is in a form selected from the group consisting of forms suitable for subcutaneous injection and forms suitable for the preparation of a form for subcutaneous injection.

5. (Withdrawn) The pharmaceutical combination of claim 1, in which the therapeutic antithrombotic agent with at least possible side effect is selected from the group consisting of anti vitamin K, antiaggregants, anticoagulants, anti thrombin, fibrinolytics and mixtures thereof.

6. (Withdrawn) The pharmaceutical combination of claim 1, in which the therapeutic antithrombotic active agent with possible side effect and glycine betaine are in a form selected from the group consisting of a form suitable for simultaneous administration, a form suitable for successive administration, and a form suitable for administration according to different administration paths.

7. (Withdrawn) The pharmaceutical combination of claim 1, in which the therapeutic antithrombotic active agent has at least one possible haemorrhagic side effect, and in which the combination comprises a therapeutically effective amount of glycine betaine for completely preventing said haemorrhagic side effect.

8. (Withdrawn) A method of preventing side effects associated with an active agent selected from the group consisting of anti aggregants selected from the group consisting of abciximab, acetylsalicylate basic aluminium, acetylsalicylate carbonate sodium, acetylsalicylate lysine, acetylsalicylic acid, aloxiprine, anagreli chlorydrate, bencyclane furamate, carbasalate calcium, clopidogrel sulfate, epoprostenol sodium, epifibati, hydroxychloroquine sulfate, iloprost, nicergoline, nifepidine, pyricarbate, sulfinpyrazone, ticlopidine chlorhydrate, tirofiban chlorhydrate, verapamil chlorhydrate, compounds structurally similar to one of the preceding anti aggregant compounds, and mixtures thereof, anticoagulants selected from the group consisting of acenocoumarol, anisindione, biscoumacetate ethyl, bromindione, coumetarol, dalteparine sodium, sirudine, xtran sulfate, enoxaparine sodium, fluindione, heparinate magnesium, heparin calcium, heparine sodium, lepirudine nadroparine calcium, oxazidione, pentosane polyester sulfuric, phenindione, phenprocoumone, reviparine sodium, tinzaparine sodium, tioclomarol, warfarine sodium, glycoaminoglycans, heparins, unfractioned heparin, standard heparin, low molecular heparins, heparinoids, heparin-like molecules, compounds structurally similar to one of the preceding anti coagulant compounds, and mixtures thereof, fibrinolytics selected from the group consisting of altepase, anistreplase, atorvastatine calcium, bromelaines, ciprofibrate, defibrotide, fluvastatine sodium, glicazide, lovastatine, lys-plasminogene, phenformine, pravastatine sodium, reteplase, simvastatine, streptokinase, urokinase, compounds structurally similar to one of the preceding fibrinolytic compounds, and mixtures thereof, thrombin inhibitors such as argatroban, novastan, and mixtures thereof, anti vitamin K, and mixtures thereof, said method comprising the step of:

administering an antidote composition comprising an active antidote agent compound selected from the group consisting of glycine betaine, compounds of the formula $(CH_3)_3N^+(CH_2)_nCOO^-$ with n being an integer from 1 to 5, pharmaceutically acceptable salts of said compound, esters of said compound, precursors of said compound, and mixtures thereof.

9. (Withdrawn) A method of preventing or reducing the incidence or severity of a side effect of a therapeutically active agent having at least one possible haemorrhagic side effect in a patient comprising the step of:

administering to said patient an effective amount of a compound selected from the group consisting of compounds having the formula $(CH_3)_3N^+(CH_2)_nCOO^-$ with n being an integer from 1 to 5, pharmaceutically acceptable salts of said compound, esters of said compound, precursors of said compound, and mixtures thereof, said administration preventing or reducing the incidence or severity of said side effect or potentialising the therapeutic effect of said therapeutically active agent.

10. (Withdrawn) The method of claim 9, said compound comprising glycine betaine, and said administration of said compound preventing or reducing the incidence or severity of said side effect and potentializing the therapeutic effect of said therapeutically active agent.

11. (Withdrawn) A method of potentializing the therapeutic effect of a therapeutically active agent having at least one possible haemorrhagic side effect in a patient comprising the step of:

administering to said patient an effective amount of a compound selected from the group consisting of glycine betaine, compounds having the formula $(CH_3)_3N^+(CH_2)_nCOO$ with n being an integer from 1 to 5, pharmaceutically acceptable salts of said compound, esters of said compound, precursors of said compound, and mixtures thereof.

12. (Withdrawn) A method of treating or preventing thrombosis troubles for a patient and preventing or reducing a haemorrhagic side effect comprising the steps of:

administering to said patient a therapeutically effective amount of an anti thrombotic active agent with at least one possible haemorrhagic side effect; and

administering a therapeutic effective amount of glycine betaine to said patient and thereby preventing or reducing said haemorrhagic side effect.

13. (Withdrawn) The method of claim 12 said glycine betaine being subcutaneously injected.

14. (Currently Amended) A controlled release pharmaceutical system suitable for delivering after administration in a time-controlled manner to the bloodstream of a mammal comprising an effective amount of an active compound selected from the group consisting of ~~glycine betaine~~ <u>a compound of the formula $(CH_3)_3N^+(CH_2)_nCOO^-$, with n equal to 1</u>,pharmaceutically acceptable salts thereof, and mixtures thereof.

15. (Original) The system of claim 14, said system being selected from the group consisting of oral controlled release preparations, oral controlled release devices, transdermal controlled release preparations, transdermal controlled release devices, and combinations thereof.

16. (Original) The system of claim 14, said system operable for releasing glycine betaine as an active ingredient.

17. (Previously Presented) The system of claim 14 wherein said system comprises at least one electronic element selected from the group consisting of an electronic device and chip, said at least one element operable for controlling at least the releasing of the active compound.

18. (Original) The system of claim 14, said system controlling delivery of said compound for at least about 120 minutes.

19. (Currently Amended) A controlled release pharmaceutical system for achieving a goal selected from the group consisting of treating a condition, reducing the incidence of a condition, reducing the severity of a condition, and preventing a condition, whereby said condition is selected from the group consisting of blood flow disturbances, thrombosis, thromboembolic disorders, and combinations thereof, said system being adapted for releasing in a time controlled manner for at least 120 minutes, after administration, a therapeutically effective amount of an active compound selected from the group consisting of ~~glycine betaine~~ a compound of the formula $(CH_3)_3N^+(CH_2)_nCOO^-$, with n equal to 1, pharmaceutically acceptable salts of said compound, and mixtures thereof.

20. (Previously Presented) The system of claim 19 wherein said system comprises at least one electronic device or chip, said at least one electronic element selected from the group consisting of an electronic device and chip, said at least one electronic element being operable for controlling at least the release of the active compound.

21. (Original) The system of claim 19, said system being an oral controlled release pharmaceutical system.

22. (Previously Presented) The system of claim 19 wherein said system comprises at least one electronic element selected from the group consisting of an electronic device and chip, said element being operable for controlling the release of the active compound.

23. (Previously Presented) The system of claim 19, wherein the system is adapted for controlling the release of said active compound for at least for 180 minutes.

24. (Previously Presented) The system of claim 19, wherein the system is adapted for controlling the release of said active compound for at least for 240 minutes.

25. (Previously Presented) The system of claim 19, wherein the system is adapted for controlling the release of said active compound for at least for 360 minutes.

26. (Cancelled)

27. (Currently Amended) A controlled release pharmaceutical system for releasing an effective therapeutic amount of a compound selected from the group consisting of ~~betaines~~ a compound of the formula $(CH_3)_3N^+(CH_2)_nCOO^-$, with n equal to 1, pharmaceutically acceptable salts thereof, precursors thereof, and mixtures thereof, wherein said system is adapted for controlling for at least 120 minutes the release of an effective amount of a compound of glycine betaine, pharmaceutically acceptable salts thereof, and mixtures thereof.

28. (Previously Presented) The system of claim 27, in which the system is adapted for controlling at least for 180 minutes the release of an effective amount of a compound selected from the group consisting of glycine betaine, pharmaceutically acceptable salts thereof, and mixtures thereof.

29. (Previously Presented) The system of claim 27, in which the system is adapted for controlling the release of an effective amount of a compound selected from the group consisting of glycine betaine, pharmaceutically acceptable salts thereof, and mixtures thereof for a time period of from about 240 minutes to 2160 minutes.

30. (Previously Presented) The system of claim 27 wherein said system comprises at least one electronic element selected from the group consisting of an electronic device and chip, said element being operable for controlling the release of the active compound.

31. (Withdrawn) A method for treating, reducing the incidence or severity of, or preventing a condition selected from the group consisting of blood flow disturbances, thrombosis, thromboembolic disorders, and combinations thereof, said method comprising the step of administering in a time controlled manner to the bloodstream of a mammal, a therapeutically effective amount of an active selected from the group consisting of glycine betaine, a compound of the formula $(CH_3)_3N^+(CH_2)_nCOO^-$ with n equal to 1, pharmaceutically acceptable salts of said compound, esters of said compound, precursors of said compound, and mixtures thereof.

32. (Withdrawn) The method of claim 31, said administration being transdermal.

33. (Withdrawn) A pharmaceutical combination for oral, parenteral or rectal administration comprising:

a therapeutically effective amount of a therapeutically active agent causing at least one haemorrhagic side effect, said active agent being selected from the group consisting of dalteparine sodium, sirudine, xtran sulfate, enoxaparine sodium, fluindione, heparinate magnesium, heparin calcium, heparine sodium, lepirudine nadroparine calcium, pentosane polyester sulfuric, reviparine sodium, tinzaparine sodium, glycoaminoglycans, heparins, unfractioned heparin, standard heparin, low molecular heparins, heparinoids, heparin-like molecules, compounds structurally similar to one of the preceding anti coagulant compounds, and mixtures thereof; and

a therapeutically effective amount of a compound selected from the group consisting of glycine betaine, $(CH_3)_3N^+(CH_2)_nCOO^-$ with n being an integer from 1 to 5, pharmaceutically acceptable salts thereof, esters thereof, precursors thereof, and mixtures thereof,

said combination preventing or reducing the incidence or severity of said haemorrhagic side effect or potentialising the therapeutic effect of said active agent.

34. (Withdrawn) The pharmaceutical combination of claim 33, wherein said therapeutically active agent has at least possible haemorrhagic side effects, and in which said combination comprises a therapeutically effective amount of glycine betaine for preventing or reducing the incidence or severity of said haemorrhagic side effect.

35. (Withdrawn) The pharmaceutical combination of claim 33, said glycine betaine being in a form suitable for subcutaneous injection or in a form suitable for the preparation of a form for subcutaneous injection.

36. (Withdrawn) The pharmaceutical combination of claim 33, said combination preventing or reducing the incidence or severity of said haemorrhagic side effect and potentialising the therapeutic effect of said active agent.

37. (Withdrawn) The pharmaceutical combination of claim 33, said therapeutically active agent being an antithrombotic agent with possible side effects, and said glycine betaine and said therapeutically active agent each being in a form suitable for simultaneous administration or successive administration or for administration according to different paths.

38. (Withdrawn) A method of treating a patient comprising the steps of:

administering to said patient an effective amount of a therapeutic active agent with at least one possible haemorrhagic side effect, and

administering to said patient an effective amount of a compound selected from the group consisting of compounds of the formula $(CH_3)_3N^+(CH_2)_nCOO^-$ with n being an integer from 1 to 5, pharmaceutically acceptable salts thereof, esters thereof, precursors thereof, and mixtures thereof, wherein administration of said compound prevents or reduces the incidence or severity of said at least one side effect of said therapeutically active agent or potentializes the therapeutic effect of said therapeutically active agent.

39. (Withdrawn) The method of claim 38, said compound comprising an effective amount of glycine betaine.

40. (Withdrawn) A method for treating or preventing at least one trouble selected from the group consisting of blood flow disturbance, thrombosis, thromboembolic disorders and combinations thereof comprising the step of administering to the bloodstream of a mammal in a controlled manner a therapeutically effective amount of a compound selected from the group consisting of glycine betaine, compounds of the formula $(CH_3)_3N^+(CH_2)_nCOO^-$ with n being an integer from 1 to 5, pharmaceutically acceptable salts thereof, esters thereof, precursors thereof, and mixtures thereof.

41. (Withdrawn) The method of claim 40, said administration being transdermal.

42. (Currently Amended) A controlled release pharmaceutical system for achieving a goal selected from the group consisting of treating a condition, reducing the incidence of a condition, reducing the severity of a condition, and preventing a condition, whereby said condition is selected from the group consisting of blood flow disturbances, thrombosis, thromboembolic disorders, and combinations thereof, said system being adapted for releasing in a time controlled manner for at least 2160 minutes, after administration, a therapeutically effective amount of an active compound selected from the group consisting of ~~glycine betaine~~ a compound of the formula $(CH_3)_3N^+(CH_2)_nCOO^-$, with n equal to 1, pharmaceutically acceptable salts thereof, and mixtures thereof.

Remarks:

Claims 14-25, 27-30, and 42 remain for consideration in this application with claims 14, 19, 27, and 42 being in independent format. Claims 14, 19, 27, and 42 have been amended and claims 1-13 and 31-41 have been withdrawn pursuant to a restriction requirement. Claim 26 has been previously cancelled.

Independent claims 14, 19, 27, and 42 have been amended to recite "a compound of the formula $(CH_3)_3N^+(CH_2)_nCOO^-$, with n equal to 1" in lieu of the term "glycine betaine." This formula was previously recited in the claims as originally filed; however, it was subsequently deleted because once the claims were amended to limit "n" to 1, Applicant considered the structure redundant with the term "glycine betaine." However, in order to clarify for the Examiner the intended compounds, Applicant has reintroduced this structural formula into the claims.

As an initial matter, Applicant notes that the Office Action Summary sheet indicates that the Action is both Final and Non-final. Applicant's representative spoke with Examiner Betton on October 20, 2008, who clarified that the Action was intended to be Non-final. Applicant respectfully requests confirmation of this in the next communication.

Turning to the Office Action, Applicant notes with appreciation that the previous written description rejection and the rejections based upon U.S. Patent No. 6,287,765 and U.S. Pat. App. Pub. No. 2002/0034757, both to Cubicciotti et al. and U.S. Patent No. 6,399,785 to Murphy et al. (hereinafter "Murphy") have been withdrawn.

However, the Examiner has rejected claims 14-25, 27-30, and 42 as being obvious in view of the combined teachings of five references: U.S. Patent No. 4,605,548 to Ushiyama et al.

(hereinafter "Ushiyama"), U.S. Patent No. 5,405,614 to D'Angelo et al. (hereinafter "D'Angelo"), U.S. Patent No. 5,814,599 to Mitragotri et al. (hereinafter "Mitragotri"), U.S. Patent No. 4,911,916 to Cleary, and U.S. Patent No. 5,928,195 to Malamud et al. (hereinafter "Malamud"). Each of these references is newly cited in this Office Action, with the exception of Malamud, which was cited in the previous Office Action.

According to the Examiner, Ushiyama discloses a transdermal drug delivery system, while an electronically-based transdermal drug delivery is disclosed in D'Angelo. The Examiner concedes that neither Ushiyama nor D'Angelo teaches or suggests glycine betaine. The Examiner further states that D'Angelo "does not provide reasoning as to why it would be pharmaceutically advantageous to incorporate glycine betaine...into a transdermal drug delivery system." Office Action, page 7. However, the Examiner argues that the deficiencies of D'Angelo are resolved by the teachings of Mitragotri. Specifically, the Examiner asserts that although Mitragotri does *not* teach glycine betaine, it does teach that hydrophilic molecules have enhanced transdermal penetration (the Examiner then notes that based upon Applicant's specification glycine betaine is a hydrophilic compound). Next, the Examiner points to Cleary as teaching drug compatibility studies and states that based upon the combined teachings of Mitragotri and Cleary, it would be desirable to cover glycine betaine with a hydrophobic polymer for more effective transdermal administration. Importantly, at the top of page 8 of the Office action, the Examiner acknowledges that ***none of the above references teach "glycine betaine."*** However, the Examiner states that the teaching of "glycine betaine" comes from Malamud, which discloses a "betaine compound." The Examiner then asserts that the term betaine is interchangeable with the term glycine betaine (citing col. 5, line 38

of Malamud). Finally, at the end of the rejection, the Examiner argues that the effects observed with the mixtures in Malamud containing both glycine and betaine would be same as those observed with glycine betaine. Thus, the Examiner concludes that all of the claims are *prima facie* obvious in view of the combined teachings of these five references.

Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness in view of these references, and further that even if one had been established, Applicant has effectively rebutted a *prima facie* showing of obviousness with objective, empirical evidence. When claims are rejected as obvious in view of two or more references, a holding of obviousness must be based on "an apparent reason to combine the known elements in the fashion claimed." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. ___, 82 U.S.P.Q.2d 1385, 1396 (2007). That is, "either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references." *Ex parte Clapp*, 227 U.S.P.Q. 972, 973 (B.P.A.I. 1985). Mere conclusory statements cannot sustain an obviousness rejection as there must be "some *articulated reasoning* with some *rational underpinning* to support the legal conclusion of obviousness." *In re Kahn*, 441 F.3d 977, 988, 78 U.S.P.Q.2d 1329 (Fed. Cir. 2006) (emphasis added) (*cited with approval in KSR*, 550 U.S. at ___, 82 U.S.P.Q.2d at 1396). Moreover, if the proposed modification or combination would render the prior art invention unsuitable for its intended purpose, or change its principle of operation, then there can be no suggestion or motivation to make such modification or combination. *In re Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984).

The present claims are directed towards controlled release pharmaceutical systems which include an effective amount of a compound selected from the group consisting of "a compound of the formula $(CH_3)_3N^+(CH_2)_nCOO^-$, with n equal to 1, pharmaceutically acceptable salts of said compound, and mixtures thereof." None of the cited prior art references teach or suggest a compound having the recited structure, pharmaceutically acceptable salts thereof, and mixtures thereof, as claimed. That is, the Examiner has already acknowledged that there is no teaching of "glycine betaine" in Ushiyama, D'Angelo, Mitragotri, or Cleary. Rather, the Examiner relies solely on Malamud for the teaching of the glycine betaine. However, as explained in detail below, Malamud discloses only an "alkyl-*N*-betaine surfactant" or "alkyl dimethyl glycine" (col. 5, ll. 38; 45), neither of which teach or suggest the claimed compound.

In the previous response, Applicant submitted a Declaration under 37 C.F.R. § 1.132 by Dr. Christian Grandfils, Ph.D., Assistant Professor at the University of Liège in Belgium. As explained in the Declaration, Dr. Grandfils has a Ph.D. in Biomedical and Experimental Sciences from the University of Liège, Belgium, and is currently an Assistant Professor and a member of the medicine faculty at the University of Liège. He is also the Director of the Interfacultary Center for Biomaterials (CEIB) at the University, and has spent the past 30 years researching tissue engineering, drug delivery systems, optimization of diagnostic systems, and *in vitro* biocompatibility testing of biomaterials. Thus, Dr. Grandfils is clearly an expert in this field.

In the Declaration, Dr. Grandfils explained the structural, chemical, and physio-chemical differences between the alkyl-*N*-betaine compounds disclosed in Malamud and the claimed compound. He further attested that because of these differences, a person of ordinary skill in the art

would not have found the claimed compounds to be obvious or predictable based upon the teachings of Malamud.

In more detail, Dr. Grandfils explained that Malamud is directed towards the delivery of microbicidal drugs comprising surfactants with spermicidal, antiviral, antibacterial, and antifungal activities, such as alkyl-*N*-betaine surfactants, in combination with an oxide. According to Dr. Grandfils, the drug's activity is centered on the association of the surfactant with the oxide to form a stable micellar structure in the compound. Dr. Grandfils explained in detail that the differences in structure between the disclosed alkyl-*N*-betaine and the claimed compound give rise to *fundamentally different and disparate physical and chemical properties*, which are neither predictable nor obvious in view of each other. For example, alkyl-*N*-betaine surfactants contain an alkyl chain, which Dr. Grandfils explained is responsible for generating the surfactant properties with the associated spermicidal, antiviral, antibacterial, and antifungal activities (i.e., the alkyl chain disrupts the cell membrane function of the microorganisms). This assessment was supported by Exhibit B, which was submitted with the Declaration (Birnie et al., *Antimicrobial Evaluation of N-Alkyl Betaines and N-Alkyl-N,N,-Dimethylamine Oxides with Variations in Chain Length*, 44 ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, 2514-2517 (Sept. 2000)). In contrast, as noted by Dr. Grandfils in the Declaration, the claimed compound *does not* exhibit microbicidal properties. Rather, it actually provides a *favorable* environment for microorganisms: (1) it has protective effects on spermatozoa; (2) it favors bacterial growth, and bacteria avidly uptake glycine betaine to protect themselves; and (3) it favors fungal growth and the development of yeast. Applicant supported these assertions with previously submitted reference materials (Exhibits E-K).

Therefore, based upon the structural and chemical differences between the claimed compound and the disclosed surfactants, Dr. Grandfils declared that a person skilled in the art would have *no reasonable expectation* that the alkyl-*N*-betaine surfactants disclosed in Malamud would be capable of generating the therapeutic properties of the claimed compound to treat thrombosis.

In summary, Applicant has already established, through objective evidence and information, that the claimed compound and the surfactants disclosed in Malamud have different chemical structures, which give rise to fundamentally different chemical and physical properties. Applicant respectfully asserts that the Examiner has improperly ignored the evidence and Declaration by Dr. Grandfils regarding Malamud and the differences between the claimed compound and the surfactants disclosed in Malamud. Moreover, the Examiner makes numerous unsupported assertions in the present Office Action, which contradict the evidence submitted by Applicant. Applicant respectfully submits that this is improper.

For example, despite Dr. Grandfils' Declaration, the Examiner continues to assert that the compounds disclosed in Malamud (i.e., mixtures containing glycine and betaine) would be expected to provide the same therapeutic effects as the claimed compound. Office Action, page 9. However, it is well know that a "presumption of obviousness based on a reference [allegedly] disclosing structurally similar compounds may be overcome where there is evidence showing there is no reasonable expectation of similar properties in structurally similar compounds." M.P.E.P. § 2144.09 (citing *In re May*, 574 F.2d 1082, 197 U.S.P.Q. 601 (C.C.P.A. 1978)). As reiterated above, in the previous response, Applicant effectively established that there would be no reasonable expectation of similar properties between the claimed compounds and the surfactants in Malamud. That is,

Applicant has demonstrated that not only would there be no reasonable expectation of similar properties, but in fact, the claimed compound and the surfactants in Malamud *do not* have similar properties (i.e., one is microbicidal, one is not). Although the Examiner believes one *might expect* the claimed compound and the compounds of Malamud to possess similar properties, Applicant effectively rebutted this presumption by showing that the compounds of Malamud do <u>not</u> have similar properties to the claimed compound.

In addition, when an Applicant has submitted evidence to rebut an allegation of obviousness, the Examiner *must* consider this evidence. M.P.E.P. § 716.01(a). "Where the evidence is insufficient to overcome the rejection, the examiner *must specifically* explain why the evidence is insufficient." M.P.E.P. § 2145. That is, if the submitted evidence is deemed insufficient, the Examiner should "specifically set forth facts and reasoning that justify this conclusion" and should avoid giving the evidence no weight, except in rare circumstances. *Id.*

Applicant respectfully submits that this has not been done in the present case. Rather, instead of reconsidering the reliance on Malamud in view of the evidence submitted by Applicant, or responding with evidence of his own, the Examiner simply dismissed the Declaration as not being persuasive. The Examiner provided no substantive response to Applicant's arguments or to the evidence presented in the Declaration, while continuing to rely on Malamud as a basis for rejecting the claims. The Examiner indicated in the Office Action that the Declaration of Dr. Grandfils was "acknowledged and made of record." Office Action, page 2. The Examiner then set forth a brief summary of his interpretation of Applicant's arguments and the Declaration. Finally, the Examiner stated that "Applicant's arguments are considered but are not found persuasive." No other discussion

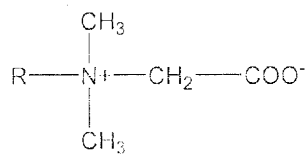
or explanation was provided for why the evidence presented in the response or Declaration was not persuasive. This is improper. *See* M.P.E.P. § 2145.

Further, it is unclear whether the Examiner actually considered the substance of the Declaration (in addition to acknowledging and recording it). For example, the Examiner stated that the "Declaration discloses that references Malamud and Murphy teach non-analogous art..." Office Action, page 2. However, Applicant respectfully submits that this is inaccurate, as there was no discussion of "non-analogous art" in the Declaration. That is, an assertion of "non-analogous art" is a legal argument, which was presented by Applicant in the remarks of the previous response. However, the Declaration by Dr. Grandfils was limited to scientific evidence and the technical knowledge of those skilled in the art pertaining to the known chemical and physio-chemical properties of the claimed compound, as compared to the compounds disclosed in the cited references. Accordingly, Applicant respectfully requests that the Examiner give meaningful consideration to the previously submitted evidence. Moreover, if such evidence is still not considered to be persuasive, Applicant respectfully requests that the Examiner provide a specific explanation in support of this conclusion.

As established above, there is no teaching or suggestion in Malamud of the claimed compound. Applicant further submits that one of ordinary skill in the art would have no motivation to modify Malamud to use the claimed compound. That is, Malamud is concerned with intravaginal delivery of microbicides comprised of an alkyl-*N*-betaine surfactant and an oxide. Malamud incorporates by reference three patents (U.S. Pat. Nos. 4,107,328, 4,839,158 and 5,314,917), which describe the preferred drugs for use in the device. Col. 5, ll. 34-43. The Examiner's attention to

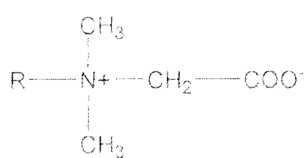
drawn to the attached Declaration signed by Jallal Messadek, the inventor named in the present application. Mr. Messadek has reviewed the patents cited by Malamud, which are discussed in the Declaration. In summary, *none* of the cited patents discloses the claimed compound. In particular, as Mr. Messadek explains in the Declaration, U.S. Patent No. 4,107,328 teaches as follows:

> "In general, a first component, namely, alkyl-N-betaine surfactant employed as a non-ionizing zwitterion can be written as:



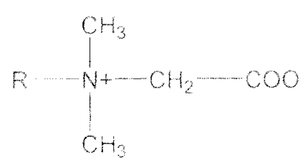
> Where R is a higher alkyl having from ***10 to 18 carbon atoms***. Illustrative of such alkyl-N-betaine is coco-N-betaine, cetyl-N-betaine, stearyl-N-betaine, isostearyl-35 N-betaine, or oleyl-N-betaine, or mixtures of the same."

Column 2, lines 23-36. U.S. Patent No. 4,839,158 discloses an "alkyl-*N*-betaine" having the structure



"where R is a higher alkyl group having from ***10 to 18 carbon atoms***." Col. 2, lines 14-49.

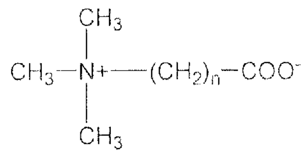
Likewise, U.S. Patent No. 5,314,917 discloses an "alkyl-*N*-betaine" having the structure



"where R is a higher alkyl group having from ***10 to 18 carbon atoms, preferably from 12-16 carbon atoms***." Col. 4, line 48 - col. 5, line 18.

The mechanism of antimicrobial alkyl-*N*-betaine surfactants rests on their ability to disturb the microorganism's membrane phospholipids. This activity is *only* seen in alkyl-*N*-betaine

surfactants having long alkyl chains, as those described in the patents disclosed in Malamud above. In contrast, the presently claimed structure (below) would not have this functionality.



, where n equals 1.

Indeed, the claimed compound actually *favors* microbial activity, as explained in the Declarations. Thus, it cannot be said that the "alkyl-*N*-betaine surfactant" disclosed in Malamud would teach or suggest to one of ordinary skill in the art to use the claimed compound because these are different compounds, with different structures, and different functionalities.

Importantly, it is noted that Malamud never discloses "betaine" alone. Rather, as Mr. Messadek points out in the attached Declaration, the term is always disclosed as an "alkyl-*N*-betaine surfactant," which, contrary to the Examiner's assertions, is *not* interchangeable with "glycine betaine," or even "betaine." Applicant respectfully submits the Examiner is mis-characterizing the prior art in an attempt to make the disclosed compounds seem closer than they really are to the claimed compound of the recited formula, pharmaceutically acceptable salts thereof, and mixtures thereof.

As shown above, these are not the same or similar compounds. If the Examiner continues to rely on the disclosure of "alkyl-*N*-betaine surfactant" in Malamud as teaching or suggesting the claimed compound, it is respectfully requested that the Examiner provide scientifically-based reasoning and explanation to rebut Applicant's arguments. In particular, it is requested that the Examiner explain how one of ordinary skill in the art would have arrived at the claimed compound

from the particularly drawn structures for the "alkyl-N-betaine surfactants" disclosed expressly and by reference in Malamud, despite the known physical and chemical differences between these compounds. Simply dismissing Applicant's arguments as "not being persuasive" is insufficient to meet the Examiner's requisite burden when considering substantive evidence submitted by an Applicant. *See* M.P.E.P. § 2145.

Finally, the Examiner's attention is again directed to the previously submitted Declaration of Dr. Grandfils and Exhibit B (article by Birnie, et al., coauthored by Malamud). In the Declaration, Dr. Grandfils avers that there would be no scientific rationale to modify the surfactants disclosed in Malamud to remove the alkyl chain and replace it with a methyl group to arrive at the claimed compound structure. That is, removing the alkyl chain from the betaine surfactant in Malamud would defeat the spermicidal, antiviral, antibacterial, and antifungal activities of the surfactant and render the drug unsuitable for the intended microbicide purposes disclosed in Malamud. This is especially true in light of Birnie et al. above, which teach away from this modification by teaching that *longer* alkyl chains are preferred as they demonstrate better antimicrobial activity.

Specifically, on page 2515 under the Results section, Birnie et al. disclose that "Antimicrobial activity was very poor at lower chain lengths." The "lower chain lengths" referred to in Birnie et al. correspond to C_8 chain lengths, which were the shortest chain lengths even tested. Moreover, as shown in Table 2, higher chain lengths of C_{12}-C_{18} performed exponentially better. Thus, it cannot be said that one of ordinary skill in the art would have been motivated to replace the higher chain lengths in the alkyl-*N*-betaine surfactants disclosed in Malamud with the methyl group

of the claimed compound, as this would change the principle of operation of the microbicidal compounds used in Malamud (i.e., they would no longer be microbicidal).

This modification would also interfere with the surfactant's interaction with the oxide and inhibit the formation of the micellar structure necessary to create a stable microbicide compound. That is, as previously explained, the formation of the micellar structure is based upon the long alkyl chain on the surfactant, which would no longer be present to form the stable structure if the alkyl-*N*-betaine surfactant is replaced by the claimed compound. Thus, because the proposed modification would render the invention of Malamud unsuitable for its intended purpose, or change its principle of operation, there can be no suggestion or motivation to make such modification. *In re Gordon*, 733 F.2d at 902.

As Mr. Messadek summarizes in the attached Declaration, to arrive at the claimed compound, one of ordinary skill in the art would have had to ignore the state of the art regarding the use of alkyl-*N*-betaine surfactants according to the above formulas where R is a higher alkyl having from 10 to 18 carbon atoms, and ignore that such long alkyl chains are responsible for the microbicidal effects of the surfactant, as stated by Malamud himself, and clearly established by the published art (Exhibit B, page 2515, Discussion 2nd paragraph). One of ordinary skill in the art would have then had to select a compound below the cutoff for microbicidal efficacy as defined by Malamud and replace the higher alkyl chain having from 10 to 18 carbon atoms with a methyl group having only 1 carbon atom. Further, one of ordinary skill in the art would have to ignore that the resulting compound (glycine betaine) is known to *favor* bacterial and microbial growth and provides the ***opposite*** properties of those sought in Malamud. Finally, this information would have had to be combined

with four additional references to arrive (allegedly) at the claimed invention. Applicant respectfully submits that there would have been no such motivation for the many reasons already stated. Accordingly, Applicant respectfully submits that the claimed invention would not have been obvious to a person skilled in the art at the time of the invention, and independent claims 14, 19, 27, and 42 are therefore patentable over the art of record.

In addition, while dependent claims 15-18, 20-25, and 28-30 recite additional patentable features, these claims should also be in condition for allowance, as depending from patentable independent claims. *In re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988).

In view of the foregoing, it is believed that no further issues exist with respect to this application. The Applicant respectfully requests a Notice of Allowance. Any additional fees due in conjunction with this amendment should be applied against our Deposit Account No. 19-0522.

Respectfully submitted,

By Tracy Bornman

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ATTORNEYS FOR APPLICANT(S)

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NOTICE OF ALLOWANCE AND FEE(S) DUE

23589 7590 06/12/2009

HOVEY WILLIAMS LLP
10801 Mastin Blvd., Suite 1000
Overland Park, KS 66210

EXAMINER	
BETTON, TIMOTHY E	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 06/12/2009

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/635,048	08/04/2003	Jallal Messadek	31927-CIP2	6961

TITLE OF INVENTION: GLYCINE BETAINE AND ITS USE

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	$755	$300	$0	$1055	09/14/2009

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

JUN 15 2009

ENTERED BY

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together .h applicable fee(s), to: Mail **Mail Stop ISS FEE**
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P.O. Box 1450
Alexandria, Virginia 22313-1450
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

23589 7590 06/12/2009

HOVEY WILLIAMS LLP
10801 Mastin Blvd., Suite 1000
Overland Park, KS 66210

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)

(Signature)

(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/635,048	08/04/2003	Jallal Messadek	31927-CIP2	6961

TITLE OF INVENTION: GLYCINE BETAINE AND ITS USE

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	$755	$300	$0	$1055	09/14/2009

EXAMINER	ART UNIT	CLASS-SUBCLASS
BETTON, TIMOTHY E	1617	514-561000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
   - ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
   - ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
   (1) the names of up to 3 registered patent attorneys or agents OR, alternatively,
   (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

   1 ______
   2 ______
   3 ______

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:
- ☐ Issue Fee
- ☐ Publication Fee (No small entity discount permitted)
- ☐ Advance Order - # of Copies ______

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ☐ A check is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number ______ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.
- ☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature ______ Date ______

Typed or printed name ______ Registration No. ______

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Notice of Allowability	Application No. 10/635,048	Applicant(s) MESSADEK, JALLAL	
	Examiner TIMOTHY E. BETTON	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to _22 October 2008_.

2. ☒ The allowed claim(s) is/are _14-15 ,17-19,21-25,27-30 and 42 (re-numbered as claims 1-15)_.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   a) ☐ All b) ☐ Some* c) ☐ None of the:

   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.

   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached

   1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.

   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date See Continuation Sheet
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

TEB	

Continuation of Attachment(s) 3. Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date: 2 sheets, 2/23/2008; 1 sheet 3/28/2009.

Interview Summary	**Application No.**	**Applicant(s)**	
	10/635,048	MESSADEK, JALLAL	
	Examiner	**Art Unit**	
	TIMOTHY E. BETTON	1617	

All participants (applicant, applicant's representative, PTO personnel):

(1) *TIMOTHY E. BETTON*. (3)_____.

(2) *Tracy L. Bornman*. (4)_____.

Date of Interview: *02 June 2009*.

Type: a)☒ Telephonic b)☐ Video Conference
c)☐ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☒ No.
If Yes, brief description: _____.

Claim(s) discussed: *14-19,21-25,27-30 and 42*.

Identification of prior art discussed: *n/a*.

Agreement with respect to the claims f)☒ was reached. g)☐ was not reached. h)☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *Discussion with Atty Bornman was drawn to the amendments to the claims as disclosed. Specifically in claims 28 and 29, it was suggested to replace the term glycine betaine with the specific chemical name as disclosed in claim 14. Further suggestions included the deletion of ' precursors thereof' and the 'and preventing a condition' in the claims found to be allowable*.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

TEB

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Tracy L. Bornman on 2 June 2009.

The application has been amended as follows:

1. Delete 1-13, 16, 20, and 26, 31-41.

2. In claim 19, line 3 before the term *reducing* **insert** "**and**".

3. In claim 19, line 3 after *condition* **delete** "**, and preventing a condition**".

4. In claim 27, line 4 after *thereof,* **delete** "**precursors thereof,**".

5. In claim 28, line 3 **delete** "glycine betaine" and **insert** "a compound of formula $(CH3)3N+(CH2)n\ COO^-$ with n being an integer of 1.

6. In claim 29, line 3 **delete** "glycine betaine" and **insert** "a compound of formula $(CH3)3N+(CH2)n\ COO^-$ with n being an integer of 1.

7. In claim 42, line 3, before *reducing* **insert** "**and**".

8. In claim 42 line 3, after the term *condition* delete " **and preventing a condition,**".

The following is the Examiner's statement of reasoning for allowance:

Reasons for allowance are supported by a lack of supportive evidence in the prior art (principally, Malumud et al. USPN 5,928,195) which discloses alkyl N-betaine in an embodiment

which does not fairly teach the glycine betaine in a controlled release pharmaceutical system suitable for delivering after administration [..] of applicants' current invention.

Specifically, Malumud teach [...] a class of compounds comprising as a first component ***an alkyl-N-betaine surfactant*** and as a second compound an oxide selected from the group consisting of alkyl-N, N-dimethyl amine oxide, N-dihydroxyethylamine oxide, acylamino t-amine oxide and mixtures thereof, as disclosed in U.S. Pat. Nos. 4,107,328, 4,839,158 and 5,314,917, the disclosures of which are hereby incorporated herein by reference [...] (column 5, lines 37-43). In view of this disclosure, the teachings, methods, and modifications of Malumud are determined to be non-sufficient in obviousness over the limitations disclosed in the current claim set. Malumud by way of several other references incorporated *supra* within this paragraph teach ***alkyl-N-betaine***, wherein the alkyl groups are C10 or higher. This modified chemical moiety would not have been obvious over $(CH3)3N+(CH2)n\ COO^{-}$ with n being an integer of 1.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance".

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY E. BETTON whose telephone number is (571)272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TEB

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617